Autologous Retinal Pigmented Epithelial Cells Derived from Induced Pluripotent Stem Cells for the Treatment of Atrophic Age Related Macular Degeneration

Grant Award Details

Autologous Retinal Pigmented Epithelial Cells Derived from Induced Pluripotent Stem Cells for the Treatment of Atrophic Age Related Macular Degeneration

Grant Type: Early Translational I

Grant Number: TR1-01219

Project Objective: The overall goal of this proposal is to develop a method for generating autologous RPE from iPSC in order to treat AMD. Intermediate goals are to explore use of an episomal vector to generate iPSC and to identify synthetic small molecules to enhance both iPSC and RPE production. The RPE will be tested for efficacy and safety in a rat model of RPE dysfunction.

Investigator:

Name:	Martin Friedlander
Institution:	Scripps Research Institute
Type:	PI

Disease Focus: Aging, Vision Loss

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: $5,806,321

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Autologous Retinal Pigmented Epithelial Cells Derived from Induced Pluripotent Stem Cells for the Treatment of Atrophic Age Related Macular Degeneration

Public Abstract: The leading cause of visual loss in Americans over the age of 65 is age related macular degeneration (AMD) which occurs in both a "wet" and a "dry" form. Both forms of the disease are associated with loss of cells called retinal pigmented epithelium (RPE) which can lead to profound loss of central vision. Currently, there is no treatment that will reverse or prevent the loss of these cells and associated blindness. Nutritional supplementation with antioxidants, macular pigments and long chain PUFAs was shown to slightly reduce disease progression but the clinical reality is that 6-8% of people over the age of 75 are legally blind from this disease. Others have observed that RPE cells can be obtained from human embryonic stem cells and that these cells may be transplanted into eyes of animals with diseases that resemble human macular degeneration with RPE dysfunction. Potential problems with this approach to treating humans with this disease include the possibility that the embryonic stem cells from which the RPE are derived may be carried over into the eye and form tumors or elicit an immune response in the recipient eye since the cells are not from the same individual receiving the transplant. Recent advances in stem cell biology now make it possible to induce the formation of pluripotent stem cells (iPSC) from adult, or somatic, tissues of individuals; these cells, in turn, may be stimulated to form RPE cells. Thus, it would be possible to produce RPE cells from the skin or hair of the same individual who would receive the transplant. In order to do this, current technology requires the use of lentiviral vectors that integrate into the genetic material of the recipient cells. In addition, the efficiency with which the iPSC are formed is not very high and to produce these cells, and the derived RPE cells, it is necessary to use "feeder" cell layers and molecules derived from animals. In this research proposal, we will take advantage of novel chemistries and molecular biological techniques to develop iPSC from somatic tissues of patients with AMD and produce RPE cells that could then be used to replace damaged tissue in these patients' eyes. Using small molecules obtained from unique chemical libraries, we will enhance the efficiency of iPSC and RPE production from somatic cells and eliminate the use of animal cell "feeder" layers and supplements. Furthermore, we will use a unique procedure ("an episomal vector") to produce iPSC from somatic cells that does not require the use of potentially dangerous viruses and permanently integrated genetic material. If we are successful, a patient with early signs of AMD could come into their ophthalmologist's office, have a skin biopsy performed that could be used to obtain RPE cells that could then be transplanted into that individual's eye at a later date when their own RPE begin to degenerate, but before they have visual loss.

Statement of Benefit to California:	As the population ages, individuals are prone to develop diseases of aging that significantly impact the quality of life in the "golden years." Foremost among these diseases is age related macular degeneration (AMD), a disease that affects the tissue in the back of the eye (the retina) used for vision. The central portion of this tissue, called the macula, is most affected in AMD and can lead to loss of fine, or "reading", vision. Vision loss occurs from two principal forms of the disease; the "wet" type involving the abnormal growth of new blood vessels and the "dry" type, involving degeneration and scarring of the macula. In both forms, special types of cells under the retina, called retinal pigmented epithelial (RPE) cells degenerate and contribute to the loss of vision. It is estimated that 15-20 million Americans over the age of 65 have AMD and 10-15% of these have vision loss secondary to the disease. Geographic atrophy (the dry type) affects 0.81% of the US population, equivalent to a prevalence of approximately 300,000 in California. Another 6.12% of the population (2.2 million Californians) suffer from early-stage AMD which puts them at high risk for developing geographic atrophy within 5 years. Currently there are some drugs available to help a certain portion of patients with the "wet" form of the disease, but there are no treatments for the "dry" or atrophic, form of the disease. We propose the use of transplants of healthy RPE cells into the eyes of patients with the atrophic form of AMD; these cells would be derived from the patients own skin or hair cells after inducing the production of pluripotent stem cells which could then be stimulated to become RPE cells. If successful, this approach would potentially provide a treatment for the leading cause of vision loss in Californians over the age of 65 with cells derived from their own tissue, avoiding potential complications associated with (1) repeated injections into the eye, (2) using cells from animals or other individuals and (3) deriving cells for transplant that have been exposed to animal cells or molecules and viral genetic material. Preserving vision in the elderly population not only would immensely improve the quality of life for these individuals, but it would also greatly facilitate their ability to function independently and productively.